Conclusions: An IL-20 ELISA has been developed and further samples are being collected for analysis. Based on these findings that IL-20 is up-regulated by TSA and under epigenetic control, targeting this cytokine may be used as a potential anti-angiogenic approach in making lung cancer history.

P3-064 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Gefitinib (Gefitinat) in advanced non small cell lung cancer-a follow up observation in Indian patients

Behera, Digambar[1] Aggrawal, Ritesh[2] Aggarwal, Ashutosh N.[2] Gupta, Dheeraj[2] Jindal, Surinder K.[2] Sharma, Surech C.[2] Kapoor, Rakesh[2]

[1] LRS Institute of Tuberculosis and Respiratory Diseases, New Delhi, India [2] Postgraduate Institute of Medical Education and Research, Chandigarh, India

A number of growth-factor-receptor-targeted agents have been tried with encouraging results in patients with advanced NSCLC (Noble et al 2006). Women, non-smokers, adenocarcinoma and Asians respond better. This communication is our further experience of our earlier presentation.

Histologically proven advanced (stage IIIB or IV) non-small cell lung cancer patients earler treated with chemotherapy received gefitinib (Gefitinat) 250mg daily orally. There were 28 females (38-57 yrs) and 67 males (44-67 yrs). Fifty four were non-smokers and the remaining were smokers. Sixty two had adenocarcinoma and 33 had squamous cell carcinoma. The disease was of stage IIIB (n=58) and stage IV (n=37). The duration of gefitinib therapy varied from 20 weeks to 58 weeks with median of 29.5 weeks. The disease remained static in 66 (69%) with stabilization or improvement in the Kornofsky performance scales in 73. The mean performance status improved from 70 to 90 in 34 cases, deteriorated in 13 and in the remaining remained static at 90. There was no radiological progression in 43 cases, while 28 cases showed radiological progression. The median survival (calculated after completion of chemotherapy and start of gefitinib) was 33 weeks with 22 patients surviving beyond 1 year. The drug was well tolerated by all. Thirty three patients complained of mild skin rash (three fixed drug eruption). 29 patients had grade 1-2 diarrhoea.

We found gefitinib as beneficial The drug is well tolerated by Indian patients.This may be due to a different pharmacogenomic property of gefitinib in this population.

P3-065 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

A lead-in safety study of erlotinib combined with sutinib for the treatment of metastatic non-small cell lung cancer (NSCLC)

Blumenschein, Jr., George[1] Robert, F.[2] Melnyk, O.[3] Sutherland, Kristin C.[4] Tye, Lesley[5] Wang, Erjian[5] Chao, Richard[5] Fossella, Frank V.[1]

[1] UT MD Anderson Center, Houston, TX, USA [2] University of Alabama at Birmingham, Birmingham, AL, USA [3] Bay Area Cancer Research Group, Concord, MA, USA [4] Pfizer, Inc., New London, CT, USA [5] Pfizer Global Research and Development, La Jolla, CA, USA

Background: VEGF expression has been correlated with increased tumor angiogenesis and shortened survival in NSCLC, and inhibition of the VEGF and also the EGF signaling pathways has a demonstrated treatment benefit in this malignancy. Therefore, a treatment strategy combining agents that specifically inhibit both signaling pathways may further improve patient outcome. Sunitinib malate is an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET and FLT3, approved multinationally for the treatment of advanced renal cell carcinoma and imatinib-resistant or -intolerant gastrointestinal stromal tumor. A multicenter phase II trial of sunitinib administered on a 4/2 schedule (4 weeks on treatment followed by 2 weeks off) in recurrent advanced NSCLC demonstrated an 11% objective response rate among patients treated second- or third-line (Socinski, ESMO 2006). Here we report the results of a lead-in safety study assessing the safety and tolerability of sunitinib combined with erlotinib in locally advanced or metastatic NSCLC after failure of chemotherapy. If the safety profile of the combination is favorable, 126 patients will be randomized to sunitinib plus erlotinib or to placebo plus erlotinib in a phase II portion of the study.

Methods: The lead-in safety cohort was planned to include 10 patients evaluable for the safety and tolerability of sunitinib combined with erlotinib, with additional patients enrolled if needed to obtain adequate pharmacokinetic data. Patients were eligible if they had histologically proven, stage IIIB or IV NSCLC; had received 1 or 2 prior chemotherapy regimens, including a platinum-based regimen; measurable disease; ECOG PS 0 or 1, and adequate organ function. Treatment comprised sunitinib 37.5 mg/day continuously plus erlotinib 150 mg/day, given orally, in repeated 4-week cycles. Patients were observed for dose-limiting toxicities (DLTs) during the first 28 days of treatment.

Results: Twelve patients were treated in the lead-in cohort, with the following baseline characteristics: median age 62 years (range 47-75); 6 male; histology 9 adenocarcinoma, 1 squamous cell carcinoma, 2 other; history of smoking in 8 patients. The patients started a median of 2 cycles (range 1-5), with dose reductions in 5 patients (erlotinib, n=2; sunitinib, n=1; both, n=2). Two patients developed a DLT (both grade 3 fatigue lasting at least 7 days). Adverse events were generally mild-to-moderate in severity (grade 1/2). Seven patients experienced grade 3 adverse events that included diarrhea (n=3), fatigue (n=2), acne (n=1), anemia (n=1), dehydration (n=1), diffuse skin rash (n=1), pruritus (n=1) and paronychial inflammation (n=1); no grade 4/5 events were reported. Pharmacokinetic analyses are ongoing.

Conclusions: Sunitinib 37.5 mg/day given continuously with erlotinib 150 mg/day was safe and tolerable in this cohort of patients with advanced NSCLC. The efficacy and safety of sunitinib combined with erlotinib will be investigated further in the randomized phase II portion of this study.

P3-066 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

The potential predictive value of cyclooxygenase-2 expression and increased risk of gastrointestinal hemorrhage in advanced non-small cell lung cancer patients treated with erlotinib and celecoxib

Fidler, Mary J.[1] Argiris, Athanassios[2] Patel, Joyti D.[3] Johnson, David H.[4] Sandler, Alan[4] Villaflor, Victoria[5] Coon, John[1] Buckingham, Lela[1] Bonomi, Philip[1]

[1] Rush University Medical Center, Chicago, IL, USA [2] University of Pittsburgh, Pittsburgh, PA, USA [3] Northwestern University, Chicago, IL, USA [4] Vanderbilt University, Nashville, TN, USA [5] University of Chicago, Chicago, IL, USA

Background: In non-small cell lung cancer (NSCLC) preclinical models, celecoxib, a cyclooxygenase-2 (COX-2) inhibitor, potentiates the apoptotic and growth inhibitory effects of erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI). We designed a phase II trial to evaluate the clinical efficacy and safety of erlotinib plus celecoxib in advanced NSCLC.